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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
TON, THAIAN N	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,332	MALISSEN ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,37,38,41-44 and 46-64* is/are pending in the application.

4a) Of the above claim(s) *38,48-56 and 62-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,37,41-44,46,47 and 57-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment and Response, filed 11/15/06, has been entered. Claims 35, 37-38, 41-44 and 46-64 are pending; claims 35, 37, 41-44, 46-48, 52, 54, 57-64 are amended; claims 36, 39, 40, 45 are cancelled; claims 38, 48-56, 62-64 are withdrawn; claims 35, 37, 41-44, 46, 47, 57-61 are under current examination.

Information Disclosure Statement

Applicants' Information Disclosure Statement, filed 11/15/06, has been considered.

Election/Restrictions

Claims 38, 48-56, 62-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/22/06.

Claim Objections

Claim 47 is objected to because of the following informalities: the claim recites the term "rodent" without an article preceding the term. It is suggested that Applicants amend the claims to recite, "the rodent".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 37, 41-44, 46, 47, 57-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A transgenic mouse whose genome comprises a mouse LAT gene encoding a mouse LAT protein wherein the mouse LAT protein consists of SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), wherein the mouse is homozygous for said gene, and the mouse has a phenotype of exaggerated TH2 cell differentiation, said mutated mouse gene and cells isolated from said mouse.

The specification does not reasonably provide enablement for the breadth of the claims, which are directed to rodents have a mutated LAT gene coding for a mutant LAT protein, wherein the sequence of the mutant LAT protein differs from a wild type sequence by a single mutation of a tyrosine located at position 136 of the mouse LAT protein sequence, said rodent being homozygous for the mutant LAT gene, or being a carrier o f a null allele of the LAT gene, wherein expression of the mutant LAT protein leads to exaggerated TH2 cell differentiation; said mutated LAT gene and cells isolated from said rodent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is maintained for reasons of record, advanced on pages 3-10 of the Office action, mailed 8/15/06.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' Arguments. Applicants argue that the claim amendments obviate the prior rejection, because the specification adequately describes and

teaches one of ordinary skill how to make and used the claimed invention. In particular, Applicants argue that one of ordinary skill in the art will appreciate the results provided in the specification with mice, and that this demonstrates possession of the claimed invention and the manner of making and using the exemplifications of the disclosure may be extrapolated to different rodents without undue experimentation. See pages 9-10 of the Response. Applicants believe that the specification describes exaggerated Th2 cell differentiation, and one of ordinary skill in the art would appreciate a correlation between i) an increase of the IgE and IgG1 secretions and of eosinophilia, and ii) an increase in TH2 cell differentiation. Applicants have provided Aguado *et al.* to support this correlation. See page 10 of the Response. Applicants further provide Genton *et al.* to confirm the results in the present specification, with regard to the exaggerated TH2 cell differentiation observed in LatY136F mice. Applicants argue that these references and the specification are sufficient to show that the claims are supported by an adequate written description. See page 11 of the Response.

Response to Arguments. Applicants' arguments are considered, but are not found to be persuasive. Because Applicants have not specifically addressed their arguments with regard to the separate rejections of enablement and written description, the Examiner addresses Applicants' arguments, as they pertain to the enablement rejection and addresses Applicants' arguments, as they pertain to written description, below.

The now-amended claims recite a *rodent* having a mutated LAT gene coding for a mutant LAT protein, wherein the sequence of said mutant LAT protein differs from a wild type sequence by a single mutation of a tyrosine located at position 136 of the mouse LAT protein sequence, said rodent being homozygous for the mutated LAT gene or being a carrier of a null allele of the LAT gene, and said mutant LAT protein leads to an exaggerated TH2 cell differentiation. The breadth of the claims are non-enabling for the following reasons.

1) Phenotype Unpredictability. The Examiner provided various references in the prior Offfice action (see pages 5-9 of the Office action mailed, 8/15/06, as well as Kappell, Mullins, (1993) Houdebine, Wall, Mullins (1996), Cameron, Sigmund, Niemann, all references cited previously) with regard to the unpredictability in the observed phenotype of transgenic animals. In particular, although the art recognized that it was possible to produce transgenic animals, and even animals of a particular phenotype, the art provides sufficient teaching and reasoning as to why the resultant phenotype of a transgenic animal is not predictable. Although Applicants have amended the claims to recite "rodent", the breadth of this term is non-enabling. For example, Encyclopaedia Britannica online ("rodent" (2007). In *Encyclopædia Britannica.* Retrieved January 22, 2007, from Encyclopædia Britannica Online: http://www.search.eb.com/eb/article-9105980) provides a general definition of the term "rodent", noting that there are more than 2,050 species of rodents, that includes 27 separate families, and animals such as rats and mice, but additionally, porcupines, beavers, squirrels, marmots, pocket gophers and chinchillas. Thus, the previously cited art is germane to the instant invention with regard to the breadth of animals encompassed by the claims.

Furthermore, examples in the literature aptly demonstrate that even closely related species carrying the same transgene construct can exhibit widely varying phenotypes. Mullins (1993, cited previously) states that not all animals express a transgene sufficiently to provide a model for a disease as the integration of a transgene into different species of animal has been reported to give divergent phenotypes. For example, several animal models of human diseases have relied on transgenic rats when the development of mouse models was not feasible. Mullins (Nature, Vol. 344, 541-544, 1990) produced outbred Sprague-Dawley x WKY rats with hypertension caused by expression of a mouse *Ren-2* renin transgene. Hammer (Cell, Vol. 63, 1099-1112, 1990) describes spontaneous inflammatory disease in inbred Fischer and Lewis rats expressing human class I major

histocompatibility allele HLA-B27 and human β_2-microglobulin transgenes. Both investigations were preceded by the failure to develop human disease-like symptoms in transgenic mice expressing the same transgenes that successfully caused the desired symptoms in transgenic rats (Mullins, **EMBO J.**, vol. 8, pages 4065-4072, 1989; **Taurog**, Jour. Immunol., Vol. 141, pages 4020-4023, 1988). Mullins (1996, J. Clin. Invest. Vol. 98, pages S37-S40, cited previously) disclose that the use of nonmurine species for transgenesis will continue to reflect the suitability of a particular species for the specific questions being addressed, bearing in mind that a given construct may react very differently from one species to another.

This unpredictability is further supported by Charreau *et al.* (**Transgenic Research**, 5:223-234 (1996)) who state that production of mice doubly transgenic for the HLA-b27 and human β2-microglobulin genes failed to develop specific symptoms either spontaneously or after treatment did not result in arthritis. However, they noted that when this construct was used in rats, the rats were able to spontaneously develop arthritis (p. 228, 1st column, Autoimmunity). Furthermore, they teach that mice transgenic for the mouse Ren-2 gene have been found to have normal expression of renin in their kidney and adrenal gland, and this gene had no effect on blood pressure. Conversely, the mouse Ren-2 gene in transgenic rats caused severe hypertension, with low levels of expression of renin in the kidney and high adrenal expression. See p. 228, 2nd column. They further teach that introduction of the human renin gene into both transgenic mice and rats did not produce pathological effects. See p. 229, 1st column, 1st paragraph. Thus, it is clear from the art that introduction of a particular transgene construct may or may not produce the same phenotype in mice and rats.

Accordingly, the specification provides specific guidance with regard to the phenotype of homozygous, LAT^{Y136F} mice; however, the specification provides no guidance or teachings with regard to the resultant phenotype of the breadth of transgenic LAT^{Y136F} rodents, as encompassed by the claims. Thus, one of skill in the

art would turn to the state of the art with regard to the production of the instantly-claimed rodents; however, the state of the art is clearly unpredictable with regard to the resultant phenotype of transgenic animals, as well as transgenic rodents.

2) Homozygous v. Carrier of Null Allele. The claims recite that the rodent is homozygous or a carrier of a null allele of the LAT gene. It is presumed that Applicants intend that "the LAT gene" refers to the wild-type LAT gene. The working examples provide guidance with regard to knock-in mice that have a mutation replacing Y136 with phenylalanine (see Example 1, page 13). The specification teaches that the effects of the LATY136F mutation was only detectable after breeding the mice to homozygous or to mice carrying a null allele of the LAT gene (see page 15, lines 20-22). The specification teaches that the homozygous mice, denoted as LAT^{Y136F}, were analyzed and found to have the phenotype of exaggerated Th2 cell differentiation (see pages 17-18, bridging ¶). There is no analysis of the phenotype of the mice that are carriers of a null allele of the LAT gene. Because as stated above, one of skill in the art could not predictably achieve a specific phenotype, and there is no specific guidance or teachings with regarding the phenotype of the mice that are carriers of the null allele of the LAT gene, it would have required undue experimentation for one of skill in the art to predict the phenotype of these mice, as instantly claimed. Thus, the specification is only enabling for a homozygous mouse whose genome comprises a mouse LAT gene encoding a mouse LAT protein wherein the mouse LAT protein consists of SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), wherein the mouse is homozygous for said gene, and the mouse has a phenotype of increased TH2 cells.

3) Residue Mutation. The Examiner maintains that one of skill in the art could not rely upon the state of the art with regard to changing any residue to produce a protein with the same function. Seffernick and Witkowski (both cited previously) provide teachings to show that one of skill in the art could not predict

the change of any particular amino acid residue and the resultant functional change in the mutant protein. Applicants have provided no evidence, reasoning or teachings to show that mutating the tyrosine at position 136 of the mouse LAT protein sequence by replacement of any other residue, would result in a rodent that has the same properties (*i.e.*, exaggerated Th2 cell differentiation) as instantly claimed. It is further noted that the claim is directed to a rodent, wherein the mutated LAT protein referred to in the claim is the mouse LAT protein. Thus, there is a lack of teachings or guidance provided by the specification with regard to the position 136 of the mouse LAT protein sequence, and correlation to the same position in any rodent LAT protein sequence, other than the exemplified mouse sequence. The specification fails to provide a correlation between the two sequences.

4) Targeted Insertion. It is maintained that claim 46 is non-enabling, with regard to the targeted insertion of a transgene into a *rodent* genome. The Examiner has previously cited Moreadith and Mullins with regard to the lack of ES cells in the art, other than from the mouse. In particular, Moreadith and Mullins clearly teach that an ES cell must give rise to germline tissue or the whole animal. Applicants have not provided any specific arguments, evidence or guidance by the specification with regard to ES cells from the genus of Rodents, which as the Examiner has shown above, to be a diverse number of species. Accordingly, in view of the state of the art with regard to ES cells, and unpredictability in targeted insertion in the genome of cells other than mouse ES cells, it would have required undue experimentation for one of skill in the art to target insertion of the recited LAT transgene into the genome of any cell in order to produce any non-human transgenic animal.

5) TH2 Cell differentiation. Applicants' arguments, with regard to the phenotype of, "exaggerated TH2 cell differentiation" is found to be persuasive. In particular, the Examiner notes that Agaudo *et al.*, provided by Applicants' in the IDS, filed 11/15/06, provides post-filing evidence that the mice with the exact

mutation as Applicants' mice, have the phenotype of exaggerated TH2 cell differentiation.

The Amount of Experimentation Necessary. The claims encompass rodents having mutated LAT genes from other species. However, the specification fails to teach these embodiments, and further, fails to provide specific guidance with regard to what the phenotype of the resultant animal would be. For example, although the specification teaches mice with a mutation in the endogenous mouse LAT gene, the specification does not teach transgenic rodents whose genome comprises a transgene that encodes for a mutant pig LAT protein, wherein the mutant pig LAT protein leads to exaggerated TH2 cell differentiation. The claims encompass this breadth, because there is no requirement for the wild type sequence to be from the same species as the rodent animal. As shown above, one of skill in the art would not be able to rely upon the art for predictability with regard to the resultant phenotype of the transgenic rodent.

The claims further encompass both heterozygous rodents, rodents that are carriers of a null allele of the LAT gene are not enabled, because the specification fails to teach the phenotype of heterozygous rodents, or rodents that carry a null allele of the LAT gene. As stated above, the phenotype resulting from any particular mutation, as broadly claimed is not predictable. The specification only provides specific guidance for homozygous mice with regard to the phenotype of exaggerated TH2 cell differentiation. There is no guidance or teachings with regard to the phenotype of heterozygous mice or mice with a null allele of the LAT gene. One of skill in the art would have to practice undue experimentation to determine a nexus between a resultant phenotype and the breadth of mutation(s) encompassed by the claims. Thus, it is determined that only homozygous mice are enabled within the scope of the invention.

Accordingly, in view of the state of the art, with regard to the unpredictability in phenotype of transgenic animals, the breadth of the claims,

which encompass any mutated LAT gene and any rodent comprising said mutated LAT gene, the state of the art which shows that mutations of even one residue of a sequence can vastly change the function of a resultant protein, that the lack of guidance or teachings provided by the specification with regard to the resultant phenotype of any transgenic rodent, other than a mouse whose genome comprises a mouse LAT gene encoding a mouse LAT protein wherein the mouse LAT protein consists of SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), and the mouse has a phenotype of exaggerated TH2 cell differentiation, it would have required undue experimentation for one of skill in the art to make and use the claimed invention.

Written Description

Claims 35, 37, 41-44, 46, 47, 57-61 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for reasons of record, advanced on pages 10-12 of the Office action, mailed 8/15/06.

Applicants' Arguments. Applicants argue that the claimed invention has adequate written description. Applicants provide no other specific arguments with regard to the written description rejection.

Response. The prior rejection is maintained for the following reasons:

1) The specification provides sufficient written description for the protein encoded by SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), the specification fails to provide a written description for any other mutated LAT protein, that when used as instantly claimed, would result in the phenotype of exaggerated TH2 cell differentiation.

Applicants have now amended the claims such that they encompass rodents have a mutated LAT gene, wherein the sequence of the mutant LAT protein differs from a wild-type sequence by a single mutation of a tyrosine located at position 136 of the mouse LAT protein sequence, further embodiments are directed to cells isolated from the rodents, and mutated genes coding for a mutant LAT protein.

The specification does not provide sufficient written description for the mutant gene as now-amended, because the specification does not provide specific guidance or description with regard to a sequence that differs from any wild type sequence (not simply the LAT sequence) by a single mutation of a tyrosine at position 136 of the mouse LAT protein sequence. In particular, there is no guidance with regard to the breadth of wild-type sequences encompassed by the claims, and what the amino acid position the mutation of the tyrosine would found in, respective to the mouse LAT protein sequence.

Furthermore, specific claims (57-61), which are directed to the mutated mouse gene are not described such that one of skill in the art would acknowledge that the inventors had possession of the claimed invention, because, although directed to a "mouse gene coding for a mutant LAT protein", the mutant can differ from "a wild type sequence" (not merely the mouse LAT wild-type sequence). Thus, the mutant mouse gene could differ from any wild-type sequence, of any protein, from any species of animal, in a sequence that has a tyrosine at the 136 position. The specification does not describe these genes.

The specification only provides description for SEQ ID NO:1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine. There is no particular indication that Applicants had possession of the claimed invention. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described by the specification, and which are not conventional in the art as of Applicants' effective filing date. Possession may be shown by actual reduction to practice, clear depiction

of the invention in a detailed drawing, or by describing the invention with sufficient and relevant identifying characteristics, as it relates to the invention as a whole, such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. In the instant case, the claimed embodiments of mutant genes that encode for a mutant protein that lead to exaggerated TH2 cell differentiation, from any species of animal, mutant LAT proteins, whose sequence differs from any wild-type sequence by a single mutation of the tyrosine Y136 residue, lack a written description. The specification fails to describe which mutated LAT proteins, other than the mouse LAT protein encoded by SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), would fall into the broadly claimed genus, which, when constructed and used as claimed, would result in the functional phenotype of exaggerated TH2 cell differentiation, as instantly claimed. The skilled artisan could not envision the detailed chemical structure of all of the mutant LAT genes encompassed by the claims, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention, and a reference to a potential method of isolating it. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification only provided the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description of 35 U.S.C. 112 is severable from its enablement provision [see p. 1115].

Claim Rejections - 35 USC § 112

The prior rejection of claims 36 and 57 is withdrawn in view of Applicants' amendment to the claim which no longer recites "the phrase "corresponds to a wild-type sequence".

The prior rejection of claim 42 is withdrawn in view of Applicants' amendment to the claims, which no longer recite "tyrosine-based sequences".

The prior rejection of claims 58 and 59 is withdrawn in view of Applicants' amendment to the claims with regard to the specific mutation referred to.

The prior rejection of claims 60 and 61 is withdrawn in view of Applicants' amendment to the claims, which clarifies which sequence is referenced in the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35, 37, 41-44, 47, 58-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants provide no specific arguments with regard to the prior rejections of record. Applicants have not overcome certain of the prior rejections of record, and thus, these rejections are maintained. Each ground of rejection is addressed specifically below.

The metes and bounds of claim 35 are unclear. This is a new ground of rejection, necessitated by Applicants' amendment to the claim. In particular, the claim recites that the sequence of the mutated LAT protein differ from a "wild-type sequence". It is unclear what wild-type sequence the claim is referring to –the wild-type mouse sequence, or the wild-type sequence of the rodent that is claimed (which encompasses animals other than mice). The claim is further confusing, because it

recites that the mutant protein has a single mutation of a tyrosine located at position 136 of the mouse LAT protein sequence. In order to produce a mutation in the tyrosine, the DNA sequence must be altered. It is unclear if by this term, Applicants intend that the single mutation refers to a conserved mutation, or a polymorphism, wherein one of the three nucleotides encoding the tyrosine residue are mutated, or that the "single mutation" refers to only one nucleic acid residue that has been changed, which could allow the resultant protein to be the same as a wild-type protein. The claim is further unclear, because it recites that the rodent can be a carrier of a null allele of the LAT gene. It is unclear what the term "the LAT gene" refers to – a wild-type LAT gene from any species, the endogenous LAT gene? Claims 37, 42-44, 46 and 47 depend from claim 35.

The metes and bounds of claim 37 are unclear. This is a new ground of rejection, necessitated by Applicants' amendment to the claim. The claim refers to a rodent "according to claim 36". Claim 36 has been cancelled by Applicants' amendment. Thus, it is unclear what the limitations of the rodent of claim 36 are, or what Applicants are attempting to incorporate, with regard to the metes and bounds of claim 37. Appropriate correction is required.

The metes and bounds of claim 41 are unclear. This is a new ground of rejection, necessitated by Applicants' amendment to the claim. The claim refers to a rodent "according to claim 40". Claim 40 has been cancelled by Applicants' amendment. Thus, it is unclear what the limitations of the rodent of claim 40 are, or what Applicants are attempting to incorporate, with regard to the metes and bounds of claim 41. Appropriate correction is required.

Claim 47, as written is unclear. This rejection is maintained for reasons of record, advanced in the prior Office action. The claim recites "any progeny thereof" in line 2 of the claim. It is unclear if this refers to progeny of the germ/somatic cell, or progeny of the non-human animal. Appropriate correction is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 47 and 57-61 are rejected under 35 U.S.C. 102(a) as being anticipated by Sommers *et al.* (cited in the prior Office action). This rejection is maintained for reasons of record, advanced on page 15 of the prior Office action, mailed 8/15/06.

The claims, as amended, are directed to germ or somatic cells from the rodent according to claim 35, containing the mutated LAT gene. Further embodiments are directed to a mutated mouse gene coding for a mutant LAT protein, the sequence of which differs from a wild-type sequence by a single mutation of the tyrosine Y136 residue.

Applicants' Arguments. Applicants argue that the Sommers reference does not teach the claimed invention, because "no mature T cells were present" in the studied LAT knock-in mutant mice having a mutation of the four distal tyrosine residues. Applicants argue that the Sommers reference does not describe a LAT Y136F rodent according to the invention, having a single mutation, and does not describe or suggest that the phonotype should be observed in such a rodent, wherein the mutant LAT protein leads, on the contrary to an exaggerated TH2 cell differentiation. Applicants argue that Sommers teaches that the mutation of four distal tyrosines leads to the arrest of thymocyte development, while the presently claimed invention, which involves the single Y136fF mutation leads to exaggerated TH2 cell differentiation, and that this result is not described in Sommers. See pages 11-12 of the Response.

Response to Arguments. These arguments have been fully considered, but are not persuasive. Applicants are arguing limitations with regard to the rodent.

The instant claims are drawn to a gene and to cells. Neither the gene nor the cells would have a phenotype of exaggerated TH2 cell differentiation, as this is a phenotype of the mouse. It is further maintained that Sommers teaches the claimed invention because Applicants' amendment has not limited the mutation to a single mutation in the wild-type mouse sequence. In fact, the claim recites "a single mutation of the tyrosine Y136". Thus, this broadly interpreted to mean that there could be a single mutation in this residue, for example, at the nucleic acid level, wherein a conserved mutation produces the same resultant amino acid. Furthermore, the claim is properly interpreted such that it does not exclude other mutations in the wild-type mouse LAT gene. Because Sommers teach the mutation of four distal tyrosine residues in the mouse LAT protein, including the instantly-claimed tyrosine 136, thus, they anticipate the claimed invention.

Sommers *et al.* teach the generation of transgenic mice which have knock-in mutations of the four distal tyrosine residues of the LAT protein at positions 136, 175, 195 and 235. They particularly teach the mutation of these tyrosine residues to phenylalanine residues (see page 137, 1st ¶). They teach isolation of thymocytes from the mice (p. 137, 2nd column). The claims are directed to cells (claim 47) and mutated mouse genes (claims 57-61), none of which will have the phenotype of the non-human animal (exaggerated TH2 cell differentiation).

Thus, Sommers *et al.* provide sufficient teachings to anticipate the claimed invention, because they teach cells isolated from mice with a mutated LAT gene coding for a mutant LAT protein, and they teach a mutated mouse gene coding for a mutant LAT protein that contains the Y136F mutation encompassed by the claims. With regard to claim 61, because they teach the mutation of the Y136 reside, it would inherently contain exon7 of the mutated gene. Accordingly, Sommers *et al.* anticipate the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

thaian ton

THAIAN N. TON
PATENT EXAMINER